REMARKS

Claims 1-20, 31-36, 41-43, 46-59, 96-98, and 112-125 are pending. Each claim amendment is supported in the specification. No new matter has been added to the present application.

Priority

In the Utility Application Transmittal which was submitted at the time of filing, Applicants requested that the specification be amended by inserting the priority information before the first line. However, in order to address the Examiner's concerns, Applicants have amended the specification to include the priority information before the first line. Reconsideration and withdrawal of this priority objection are respectfully requested.

Claim Construction

Applicants have amended the claims to address the Examiner's concerns regarding claims directed to nucleic acids comprising SEQ ID NO: 5969, or polypeptides encoded thereby, which encompass the reference sequence but does not include the single nucleotide polymorphism associated with respiratory disease. Reconsideration and withdrawal of this claim construction objection is respectfully requested.

Oath/ Declaration

The oath or declaration was found defective because non-initialed and/or non-dated alterations were made to the oath or declaration on page 5 by the inventor Sunil Pandit. Applicants respectfully submit herewith a new oath or declaration with inventor Sunil Pandit's signature. Reconsideration and withdrawal of this objection is respectfully requested in view of the new oath or declaration.

Drawings

The drawings were objected to for allegedly containing illegible text. Specifically, the margins of Figures 2I, 2K, 2L, 2O, 5B, 5D, 5E, 5F, and 5G were allegedly insufficient. Applicants respectfully disagree with the draftperson's objection. However, in order to expedite prosecution of this application, applicants submit herewith new drawings of the

objected figures. Reconsideration and withdrawal of the objections to the drawings is respectfully requested.

Specification

Applicants have amended the specification as suggested by the Examiner in order to address concerns regarding hyperlinks. Reconsideration and withdrawal of this objection to the specification are respectfully requested.

Claim Objections

Claims 1, 3, 5-13, 15-20, 31-33, 35, 36, 43, 56, 58, 96, 97, 113, 115, 116, and 118-125 stand objected to for embracing non-elected subject matter. Claims 1, 3, 5-13, 15-17, 19, 20, 31-33, 35, 36, 43, 56, 58, 96, 97, 113, 115, 116, 118, 119, 122, 124, and 125 stand objected to for referring to non-elected SNPs. Applicants have amended and/or cancelled the objected claims in order to address the Examiner's concerns. Reconsideration and withdrawal of these objections are respectfully requested.

Claims 17-20 and 118-123 have been objected to for encompassing non-elected transgenic animals. Applicants have amended and/or cancelled the objected claims by reciting "isolated host cell" as suggested by the Examiner as supported in the section entitled "Vectors and Host Cells" at pages 33-39 of the instant specification. In view of these amendments which address the Examiner's concerns, Applicants respectfully request reconsideration and withdrawal of these objections.

35 U.S.C. §112 Claim Rejections

Claims 96-98 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time that the inventors had possession of the claimed invention. The specification as filed allegedly fails to provide any written description for fragments within a specific sequence having antisense activity. However, applicants have cancelled claims 96 - 98, thereby rendering the §112, first paragraph rejection of these claims moot. Reconsideration and withdrawal of the § 112, first paragraph, rejection are respectfully requested.

Claims 1-20, 41, 43, 56, 57, 96-98, 113-117, and 119-125 stand rejected under 35 U.S.C. §112, first paragraph because the specification allegedly does not reasonably provide enablement for the broad scope of the nucleic acids encompassed by the claims. Applicants respectfully traverse the Examiner's rejection.

It is respectfully submitted that some of the claims rejected by the Examiner are not currently pending in the application, *i.e.*, claims 1, 3, 6, 8, 10, 12, 13, 16, 17, 20, 41, 43, 97, 113, 116, 117, 119, 122, and 123 have been cancelled. Consequently, applicants have directed the present response to the above-cited rejection as it pertains to pending claims 2, 4, 5, 7, 9, 11, 14, 15, 18, 19, 56, 57, 96, 98, 114, 115, 120, 121, 124, and 125 only. Independent claims 2 and 5 have been amended to delete the phrase "at least one" such that there is only one single nucleotide polymorphism change from guanine to adenine at position 21 of SEQ ID NO: 5969. In view of the presently amended claims, applicants respectfully request reconsideration and withdrawal of this §112, first paragraph rejection.

Claims 31-36 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement since the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

As an initial matter, the Examiner points to MPEP 2164.01(c) for support that "enablement for a claimed pharmaceutical requires that the specification teach an enabled pharmaceutical use" (page 16 of 7/28/04 Office Action). The Examiner relies on *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 144 (Fed. Cir. 1991) for support "[w]hen a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation." However, the basis of this rejection is not applicable to the rejection of claims 31-36. The pharmaceutical composition of claims 31-36 are not limited to a recited use. Furthermore, applicants respectfully direct the Examiner's attention to MPEP 2164.01(c), middle of the last paragraph, which reads, "[i]f multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention."

Specifically, the claimed pharmaceutical compositions have multiple uses in addition to gene therapy. For example, applicants direct the Examiner's attention to page 2, line 29 through page 3, line 10 which discloses the use of the claimed nucleic acids for assaying biological samples for the presence of 12q23-qter genes; at page 3, lines 11-22 the claimed nucleic acids may be used for diagnosing diseases or determining the predisposition of a subject for having such a disease; at page 4, line 23 through page 5, line 2, the claimed nucleic acids may be used to identify chromosomal abnormalities and allelic variants/ mutations; at page 87, line 28 through page 88, line 3, the claimed invention may be used for drug screening; and at page 106, lines 6-16, transgenic animals containing a nucleic acid molecule which encodes a human 12q23-qter polypeptide may be produced for use in drug evaluation and drug discovery. As the pharmaceutical composition of claims 31-36 have additional uses in addition to gene therapy, applicants respectfully request reconsideration and withdrawal of the §112, first paragraph rejections.

It is respectfully submitted that the instant specification clearly supports the pending claims, including the claims as amended and presented herein. The claims directed to nucleic acids have been amended to address the Examiner's comments as previously set forth.

Furthermore, based upon the teachings and exemplification in the instant specification, including the description under "Pharmaceutical Compositions" at pages 90-93, "Gene Therapy" at pages 97-102, and "Animal Model" at pages 102-107, it is respectfully submitted that the skilled practitioner would indeed be able to practice the invention as claimed without undue experimentation at the time the invention was made. Given the guidance and teachings of the instant specification, combined with the knowledge among those skilled in the art, along with the description, examples and results, it is also submitted that the skilled practitioner, following the teachings of the instant specification, could practice the invention and know how to administer cytokines and co-stimulatory molecules at the appropriate levels and combinations, without undue experimentation. To be enabling under 35 U.S.C. §112, a specification must contain a description that enables one skilled in the art to make and use the claimed invention. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984). That some experimentation is necessary does not constitute lack of enablement. It is well settled that "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of

guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)).

More specifically, the specification provides guidance and teaching for the skilled practitioner to know how to administer the claimed pharmaceutical compositions of the invention. Thus, it is respectfully contended that the complete teachings of the specification, combined with the level of knowledge possessed by those having skill in the art to which the invention pertains, allows the practice of the invention as claimed without undue experimentation.

With regard to the Examiner's concern that gene therapy was not an established art at the time the invention was made and failed to have any art-recognized means of practice, it is submitted that the references cited to support the Examiner's contention are related to a different problem in the art of gene therapy. The pharmaceutical compositions comprising a complementary nucleic acid sequence may be used to block the gene of interest, *i.e.* antisense. There is sufficient description and knowledge in the art for a skilled artisan to make and use the claimed pharmaceutical compositions. Therefore, it is respectfully submitted that the type of *in vivo* administration of nucleic acids encompassed by the presently claimed invention does not involve undue experimentation by the skilled practitioner.

Claims 1-20, 31-36, 41-43, 46-59, 96-98, and 112-125 stand rejected under 35 U.S.C.§112, second paragraph as being indefinite for the phrase "a nucleic acid variant" or compositions comprising said nucleic acid variant. Applicants have deleted the term "variant" in order to address the Examiner's concerns. Reconsideration and withdrawal of this §112, second paragraph rejection is respectfully requested.

Claims 1-4, 13, 14, 33, 34, 113, 114, 119, and 120 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite in reciting that the claimed nucleic acid encodes "SEQ ID NO:111, wherein the amino acid sequence contains at least one amino acid change." Applicants have amended and/or cancelled the rejected claims in order to address the Examiner's concerns. Reconsideration and withdrawal of this §112, second paragraph rejection is respectfully requested.

Claims 5-12, 15, 16, 19, 20, 35, 36, 56, 57, 96, 97, 115, 116, 121, 122, and 124 stand rejected as being indefinite in reciting that the claimed nucleic acid comprises the nucleotide sequences as set forth in "SEQ ID NO:19, wherein the nucleic acid comprises at least one single nucleotide polymorphism." Applicants have amended and/or cancelled the rejected claims in order to address the Examiner's concerns. Reconsideration and withdrawal of the §112, second paragraph rejections are respectfully requested.

35 U.S.C. §102 Claim Rejections

Claims 1-30, 41-46, 56-529, and 112-125 stand rejected under 35 U.S.C. §102(b) as being anticipated by Buel, et al. (U.S. Patent No. 6,133,434). Applicants respectfully disagree with the Examiner's contention that Buel, et al. discloses a nucleic acid that encodes a polypeptide that is identical to the instant SEQ ID NO:111, and further comprises the SEQ ID NO:5969* arginine to histidine substitution which is identical to SEQ ID NO:19 from nucleotides 48-1896, including the 5969* G>A substitution. Applicants respectfully traverse the rejection.

Claims 1, 3, 6, 8, 10, 12, 13, 16, 17, 20-30, 41, 43-45, 96-98, 113, 116, 117, 119, 122, and 123 have been cancelled; hence, the rejection of these claims is moot. It is submitted that the cited prior art patent does not contain each and every element of applicants' reagent compositions as presently claimed. In fact, the Examiner readily admits that the nucleic acid sequence encoding a polypeptide is 99.3% identical to the instant SEQ ID NO: 111, and further admits that from nucleotide 48-1896, there is 99.5% identity. These sequences are not identical to that set forth in the nucleic acid sequence encoding SEQ ID NO: 111 or SEQ ID NO: 19, having a single nucleotide polymorphism of guanine to adenine at position 21 of SEQ ID NO: 5969.

Furthermore, a reference that merely contains substantially the same elements is insufficient to anticipate the claimed invention. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 756 F.2d 1556, 225 USPQ 253 (Fed. Cir. 1985). In fact, applicants respectfully submit that in order to anticipate a claim, the reference must teach each and every element of the claim (see MPEP 2103).

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of*

> *California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The cited prior art fails to disclose the exact nucleic acid sequence as claimed and described in the instant specification.

According to *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991), See e.g. 2 PAT. L. FUNDAMENTALS § 11:3 nn. 25, 28, 29 (2d ed. Nov. 2003), the Amgen court set forth that an invention for a gene's DNA sequence is not "conceived" until the inventor accurately knows the gene's structure to be able to distinguish it from other materials. "When an inventor is unable to envision the detailed constitution of a gene [and] a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.* until after the gene has been isolated." *Amgen*, 927 F.2d at 1206.

The court found this to be a case of simultaneous conception and reduction to practice. *Id.* at 1206. Conception of the method was judged to be insufficient. Although Fritsch had envisioned the DNA sequence, his envisioned sequence was incorrect in some positions. *Id.* (until Fritsch could envision the gene by the precise sequence, or "in terms of other characteristics sufficient to distinguish it from other genes, all he had was an objective to make an invention which he could not then adequately describe or define."). Since each and every base of a nucleic acid sequence needs to be correct, and the Buell publication reports of a sequence having 99.3 % identity to the claimed sequence, the Buell publication does not anticipate the instant claims. The claims of the instant invention are therefore not anticipated by the Buell, et al. publication of nucleic acids, vectors, host cells, kits and compositions. Thus, for the above-mentioned reasons, applicants respectfully submit that claims 1-30, 41-46, 56-529, and 112-125 are not anticipated by Buell, et al. Based on the previous arguments and what is commonly known and understood in the art, reconsideration and withdrawal of this 35 U.S.C. §102 rejection is respectfully requested.

35 U.S.C. §103 Claim Rejections

Claims 31-36 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Buell, et al., (US Patent No. 6,133,434) in view of Maniatis, et al. (Appendix A: Biochemical Techniques, in Molecular Cloning: a laboratory manual, Cold Spring Harbor Laboratory, pp.

461-462, 1983). The Examiner has alleged that it would have been obvious for one of skill in the art to dissolve the probe of Buell, et al. in a buffer pharmaceutical composition comprising the nucleic acid of the invention as taught by Maniatis, et al. Applicants respectfully traverse the rejection.

According to the Examiner, it would allegedly have been obvious to one of ordinary skill in the art to combine the probe of Buell, et al. in a buffer as described in Maniatis, et al. However, the nucleic acid reported in Buell, et al. is not what is claimed in composition of the instant invention. The Examiner points to Maniatis, et al. to describe that one skilled in the art should use a buffer, such as Tris-EDTA, such that a nucleic acid, for example that described in Buell, et al., may be easily dissolved.

It is respectfully submitted that some of the claims rejected by the Examiner are not currently pending in the application, *i.e.*, claims 32, 33, and 36 have been cancelled, and the rejections to these claims are thereby moot. Consequently, applicants have directed the present response to the above-cited rejection as it pertains to pending claims 31, 34 and 35 only. Independent claims 2 and 5 have been amended, and accordingly, depending claims 31, 34, and 35 also incorporate these amendments.

The Examiner has combined the Buell reference with the Maniatis reference, the latter of which describes a method for dissolving DNA in a solvent. The combination of Buell, et al. and Maniatis, et al. does not make obvious the composition comprising the nucleic acid as presently claimed. The primary reference (*i.e.* Buell, *et* al.) does not teach the nucleic acid sequence of SEQ ID NO: 19 with the exception that the nucleotide sequence contains a single nucleotide polymorphism of guanine to adenine at position 21 of SEQ ID NO: 5969. The Examiner attempts to reach the instant invention by combining the Buell reference with the Maniatis reference to allege the claims directed to pharmaceutical compositions with the nucleic acid of interest (*i.e.*, claims 31, 34 and 35) is obvious. However, the Buell reference does not teach or suggest the claimed invention even with the Maniatis reference. The deficiencies of Buell are not overcome with Maniatis. In fact, Buell, et al. does not describe the nucleic acid as presently claimed regardless of the carrier or buffer of Maniatis, et al. Thus, applicants respectfully request reconsideration and withdrawal of this §103 rejection.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 2976-4044US1. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2976-4044US1. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: January 28, 2005

By: _____
Evelyn M. Kwon
Registration No. 54,246

Correspondence Address:
MORGAN & FINNEGAN, L.L.P.
3 World Financial Center
New York, NY 10281-2101
(212) 415-8700 Telephone
(212) 415-8701 Facsimile